REMARKS

Applicants respectfully request entry of the Amendment and reconsideration of the claims. Claims 1 and 6-12 have been amended, and claims 2-5 have been cancelled. New claims 13-16 have been added. Claims 1 and 6-16 will be pending upon entry of this amendment. The remarks herein refer to the Examiner's comments from the Office Action mailed January 11, 2005, and the Advisory Action mailed June 16, 2005. Applicants respectfully request reconsideration of the claims and withdrawal of the pending rejections under 35 U.S.C. § 103(a).

Amendments to the Claims

Claim 1 has been amended to delete "an angiotensin converting enzyme inhibitor" and "angiotensin II receptor antagonist".

Claims 2-5 have been cancelled.

Claims 6-12 have been amended to recite "The method of claim...".

Claims 13-16 have been added. Support can be found throughout the specification, including at paragraphs 78-80 and 89-90.

Rejections under 35 U.S.C. § 103

The Examiner rejects the claims under 35 U.S.C. § 103(a) for alleged obviousness. The Examiner asserts that the claims are unpatentable over Smith et al. (WO 98/19690) in combination with Lobel (U.S. Patent No. 3,282,778) or in combination with DiPiro. The Applicants respectfully traverse the rejection.

To establish a *prima facie* case of obviousness, three criteria must be met--a suggestion or motivation to combine references, a reasonable expectation of success, and the prior art reference teaches or suggests all the claim limitations. MPEP §2143; *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). The Examiner has not established a *prima facie* case of obviousness since there is not expectation of success for the claimed combination.

Treating ischemia does not address treating a patient who already has hypertrophy

The Examiner maintains his objection of the claims for allegedly lacking obviousness over Smith *et al.* in view of DiPiro or Lobel. In the Office Action of 11 January 2005, the Examiner stated that

> Smith et al. teach that one of the causes of the microvascular events ***leading to ischemia*** in the medial temporal lobe is a moderate deficiency in vitamin B_{12} and folate, which leads to elevated homocystein levels in the plasma, because vitamin B_{12} and folate are required cofactors in the conversion of homocysteine to methione. Homocysteine can have a toxic effect on the blood vessels that ***initiate*** the pathological cascade process leading to changes in the microvasculature. **[*emphasis added*]** Office Action of Jan. 11, 2005 at p. 11-12.

The Examiner alleges that a person skilled in the art would be expected to use a compound of the pyridoxine family to treat hypertrophy. Applicants respectfully disagree and assert that the Examiner has not established an expectation of success for treating hypertrophy.

The Examiner has not established an expectation of success for the use of vitamin B_6 related compounds to treat an enlarged heart, *i.e.*, hypertrophy. Cardiac hypertrophy is the enlargement of the heart muscle as a result of pressure overloads on cardiac ventricles (*See* U.S. Patent No. 6,780,997). Pathology of hypertrophy includes remodeling of muscular and collagenous compartments of the myocardium where the accumulation of fibrillar collagen impairs myocardial stiffness (*See* U.S. Patent No. 6,610,480). Smith *et al.* teach a method for inhibiting microvascular events *leading to* ischemia. The DiPiro reference teaches that hypertrophy is a compensatory mechanism secondary to congestive heart failure, and congestive heart failure is a consequence of a variety of underlying disorders. Microvascular events leading to ischemia are upstream events that may eventually lead to hypertrophy. Ischemia may be a risk factor for developing hypertrophy, but treating ischemia does not address the pathology of a patient who already has hypertrophy. There is no indication in Smith *et al.*, DiPiro *et al.*, or Lobel that vitamin B_6 treats the pathology or symptomolgy of an enlarged heart, *i.e.*, myocardial stiffness. Applicant respectfully asserts that the Examiner has not established an expectation of success for a method of treating hypertrophy.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

CONCLUSION

In view of the above amendments and remarks, Applicants respectfully requests a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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Date: July 11, 2005

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